

Request to Waive STN 125216/0 from Referral to Blood Products Advisory Committee - Seraclone Blood Grouping Reagent Anti-S (Monoclonal)

Memorandum

Date: July 14, 2008
To: Jay Epstein, M.D.
Director, Office of Blood Research and Review
From: Elizabeth Callaghan
Acting Director, Division of Blood Applications
Subject: **Request to waive STN 125216/0 from referral to Blood Products Advisory Committee**
CC: Robert Yetter, Ph.D., Associate Director for Review Management, CBER
Diane Maloney, J.D., Associate Director for Policy, CBER

Background

STN 125216/0 is an original biologics license application (BLA) submitted by Biotest AG for Blood Grouping Reagent, Anti-S¹ (Monoclonal), under the trade name Seraclone®. Biotest AG holds Biologics Licenses for other blood grouping reagents that are formulated for automated testing. Seraclone® Blood Grouping Reagent, Anti-S (Monoclonal) is formulated for phenotyping blood specimens using manual tube agglutination methods.

Reasons for Waiving Referral to BPAC

The Division of Blood Applications in the Office of Blood Research and Review reviewed information from this application and determined that referral to the Blood Products Advisory Committee (BPAC) prior to approval was not needed for the following reasons (FDAAA [HR 3580-138 SEC. 918: REFERRAL TO ADVISORY COMMITTEE]):

- The manufacture and use of Blood Grouping Reagents from source material of monoclonal origin is well-established, widely used and well-understood. FDA licensed the first monoclonal Blood Grouping Reagents (Anti-A and Anti-B) in 1985.
- The manufacture of Biotest's Seraclone® Blood Grouping Reagent, Anti-S (Monoclonal) is similar to that of their currently licensed products, Blood

Grouping Reagents (Formulated for Automated Testing) and Anti-Human Globulin (Formulated for Automated Testing).

- The principle of the hemagglutination test dates back to 1900 when Karl Landsteiner discovered the A, B, and O blood groups. Performing the hemagglutination test using Blood Grouping Reagent, Anti-S (Monoclonal) for manual testing is thus well-understood. The S antigen, if present on the red blood cells, binds with the Anti-S in the reagent. After incubation, the cells are washed to remove excess antibody. Anti-human globulin is added and forms red blood cell agglutinates if the antibody has attached to the antigen on the red blood cells. The presence of hemagglutination indicates the presence of the S antigen.
- Biotest's Blood Grouping Reagents (Formulated for Automated Testing) and Seraclone® Blood Grouping Reagents for manual testing are both manufactured from monoclonal cell lines.
- Blood Grouping Reagent, Anti-S (Monoclonal) is for in-vitro diagnostic testing. Positive and negative controls are required to be performed with patient and donor testing to ensure the validity of the test results.
- The results of the in-house and field trial testing did not raise any concern related to safety, purity, potency, specificity, or stability.
- Review of information submitted in the BLA for Blood Grouping Reagent, Anti-S (Monoclonal) did not raise any controversial issues or pose unanswered scientific questions which would have benefited from advisory committee discussion and recommendation.
- There are no current concerns regarding the risk/benefit ratio. In fact, there is benefit in approving this product since there are few donors with anti-S suitable for use in the manufacture of polyclonal reagent. The test is most often used in confirming the S phenotype in a patient whose plasma contains anti-S and subsequently identifying blood donors who lack the S antigen in support of the patient's transfusion needs. Furthermore, a crossmatch, i.e., compatibility test, is performed prior to transfusion whenever a patient has or had anti-S in their plasma.

Letter ready comments that summarize this memo to be included in the approval letter:

We did not refer your application to the Blood Products Advisory Committee because the mechanisms of manufacturing monoclonal reagents and their use in hemagglutination testing in immunohematology are well-understood. Our review of information submitted in your BLA, including the study design and trial results, did not raise concerns or controversial issues which would have benefited from an advisory committee discussion.

¹The antigen for S is referred to as "big S" to distinguish it from its antithetical allele s that is referred to as "little s." Likewise, the antibody is referred to as "anti-big S." In the labeling, "anti-s" has a bar over the "s" to ensure that it is not confused with "S".